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Behavioral Treatment of Insomnia: Also Effective for Nocturia

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Abstract

Objectives—To evaluate changes in self-reported nocturia among community dwelling adults aged 60 and older who received behavioral treatment for chronic insomnia.

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Conflict of Interest Disclosures:

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Employment or Affiliation		X		X		X		X		X		X
Grants/Funds		X		X		X		X		X		X
Honoraria		X		X		X		X		X		X
Speaker Forum		X		X		X		X		X	X	
Consultant		X		X		X		X		X	X	
Stocks		X		X		X		X		X		X
Royalties		X		X		X		X		X		X
Expert Testimony		X		X		X		X		X		X
Board Member		X		X		X		X		X		X
Patents		X		X		X		X		X		X
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Design—Secondary analysis of an RCT of a behavioral intervention for sleep.

Setting and Participants—Of the 79 enrollees in the RCT, this analysis focused on 30 who in addition to insomnia, also reported at least one nightly episode of waking up to void

Intervention—The Brief Behavioral Treatment of Insomnia (BBTI) group received instructions on reducing time in bed and setting a regular sleep schedule. The Information control (IC) group received printed materials. Both interventions were delivered by a nurse clinician.

Measurements—Self-reported nocturnal awakenings to void assessed daily for 14 days at baseline and 4 weeks post-intervention. Participants (16 IC; 14 BBTI) who reported at least one episode of nocturia per night at baseline were included in this analysis.

Results—Among individuals with nocturia at baseline, the total number of nocturnal voids over the 14-day assessment period decreased by 6.5 [sd, 4.8] in the BBTI group compared to an increase of 1.3 [sd, 7.3] in the information only control group ($p=0.04$, effect size 0.82). After adjusting for baseline nocturia episodes, the difference remained significant ($p=.05$).

Conclusion—Among older adults with concurrent insomnia and nocturia, behavioral treatment directed solely at insomnia may also improve self-reported nocturia. Behavioral treatment of insomnia should be further investigated for its effect on nocturia among individuals with concurrent insomnia and nocturia.

Keywords

Nocturia; Elderly; Behavioral Treatment; Insomnia

INTRODUCTION

Nocturia is defined by the International Continence Society (ICS) as waking at least once nightly to void, with each void preceded and followed by sleep.¹ Its prevalence increases significantly with age, and is approximately 70% among individuals > 60 years of age.² Nocturia is an independent predictor of both insomnia (75% increased risk) and reduced sleep quality (71% increased risk),³ and there is a “dose effect”: as the number of nightly voids increase, patients experience worsening of sleep quality, increased awakenings, difficulty returning to sleep and greater levels of daytime tiredness.⁴ Nocturia and insomnia are inextricably linked, and it is often difficult to determine the direction of this relationship. Frequent awakenings, and sleep maintenance insomnia are common in the elderly.⁵ There are many reasons for this in addition to nocturia, including other sleep disorders (e.g. sleep apnea), age-related decrease in sleep continuity and depth, changes in circadian rhythms, and spending too much time in bed.^{6, 7} In addition, exogenous factors, such as medications, light or noise,^{8, 9} and endogenous factors such as pain and stress,¹⁰ may cause frequent awakenings and contribute to insomnia. Physiological and sensory hyperarousal in older adults with insomnia¹¹ may also make them more sensitive to bladder fullness and lead to frequent awakenings to void. Because individuals with insomnia may awaken for any of the aforementioned causes, perceive a full bladder, and then elect to void, nocturia can also be a result, rather than a cause of insomnia. Therefore, it may be difficult to discern clinically if

nocturia is a cause or consequence of insomnia, especially in older patients in whom comorbidity and polypharmacy are common.

Although insomnia and nocturia are mutually exacerbating conditions, the management of nocturia lacks clear guidelines addressing concurrent insomnia. The recommended treatment of nocturia in older patients includes optimizing therapy for fluid overload conditions like congestive heart failure and diabetes, and treating underlying bladder or prostate etiologies with antimuscarinics or α -blockers. Unfortunately, such agents cause adverse events and further enhance the risk of falls, fractures and mortality among older individuals with nocturia.¹² Multicomponent behavioral or lifestyle interventions to improve nocturia, mostly focused on fluid restriction, preemptive voiding, or pelvic floor muscle training have also shown promising results.^{13–16} However, to the best of our knowledge, there has been no study of behavioral treatment of insomnia that focused on nocturia as an outcome. A recently completed sleep study provided an opportunity to evaluate changes in nocturia among older adults receiving Brief Behavioral Treatment of Insomnia (BBTI). We postulated that an intervention targeting insomnia in patients with concurrent nocturia and insomnia, might not only improve sleep but also nocturia.

METHODS

Study Design

The primary study was a randomized controlled trial designed to test the short-term efficacy of brief behavioral treatment of insomnia (BBTI) compared with an information-only control (IC) among older individuals with insomnia.¹⁷ After baseline clinical evaluation, participants were randomly assigned to BBTI or IC. BBTI constitutes the core of efficacious multi-modal behavioral treatments for insomnia. BBTI focuses on sleep education, healthy sleep practices, and behavioral interventions to improve insomnia. The four main components of BBTI that address the behavioral aspect of sleep are: 1) mildly restricting time in bed (self-reported sleep time plus 30 minutes, with a minimum of 6 hours); 2) establishing a regular wake-up time every day of the week, regardless of sleep duration; 3) going to bed only when sleepy; and 4) getting out of bed if not asleep.

The information control (IC) group received three informational brochures developed and published by the American Academy of Sleep Medicine: *Insomnia, Sleep as We Grow Older*, and *Sleep Hygiene*. The articles address sleep issues in older adults and discuss behavioral interventions similar to BBTI, but offer no personalized instructions.

Participants

Study procedures have been described previously.¹⁷ Briefly, 82 older adults who met the criteria for primary insomnia in the *Diagnosis and Statistical Manual of Mental Disorders* (Fourth Edition, Text Revision (*DSM-IV-TR*))¹⁸ were recruited from the community via advertisement (n=61) and from primary care practices (n=21). The diagnosis of primary insomnia was made by self-reported questionnaires and structured clinician interviews. The criteria for insomnia included difficulty initiating or maintaining sleep for at least one month despite adequate opportunity and circumstances for sleep, as well as associated daytime

symptoms of fatigue causing impairment in social, occupational, or other important areas of functioning. Exclusion criteria were: untreated psychiatric or substance abuse disorder, recent hospitalization (within past 2 weeks), ongoing chemotherapy or other cancer treatment, and life expectancy of < 6 months. Subjects with significant cognitive impairment (Mini-Mental State Examination [MMSE] score < 24) were also excluded because it can limit an individual's ability to comply with behavioral sleep interventions, and some of the interventions (e.g., restricting time in bed) could potentially worsen their underlying condition.

Of the 82 consented participants, 79 were randomized and completed the intervention in the primary study. For the current secondary analysis, we stratified the participants using the ICS definition of nocturia by self-report at the time of recruitment (i.e., reported waking up at least once per night on the 14-day sleep diary completed at the time of inclusion). Only participants with nocturia at baseline (16 randomized to BBTI and 14 randomized to IC) were included in the current analysis. (Figure 1)

Procedures

Participants were randomly assigned to BBTI or IC by permuted block design. The BBTI intervention included two individual sessions in which a therapist met with the participant; treatment elements were presented in the first session, which lasted 45–60 minutes, and in a 30-minute reinforcement session two weeks later. Participants received 20-minute telephone calls after one and three weeks to review sleep-wake times, and adherence, and to troubleshoot any difficulties. The IC intervention included instructions to read and review publications regarding insomnia, sleep and aging, and sleep hygiene for the first session, and two weeks later, IC participants received a 10 minutes follow-up telephone call. During in-person session and telephone calls participants were encouraged to continue participation, and were referred back to the reading material for sleep-related questions. At the conclusion of the 4-week intervention period and following post-intervention assessments, the IC group was offered BBTI. The study was approved by Institutional Review Board and all participants provided written informed consent.

Clinical Assessment

Detailed demographic information and history was obtained by self-completed questionnaires and clinician-administered interviews. All subjects completed 14-day sleep diaries and all underwent actigraphy and in-home polysomnography (PSG) studies prior to treatment and 4 weeks after the start of intervention. BBTI responders were contacted 6 months later for follow-up in the primary study, but these data were not used for our secondary analyses.

Measures

The measures obtained in the primary study have been described previously in detail.¹⁷ Each subject completed a 14-day sleep diary at inclusion and during weeks 3 and 4 following the start of the intervention.¹⁹ Every morning over the 14-day period, the participants documented in the diary how many of their awakenings were to void. The sleep diary did not differentiate between a convenience void or an urge resulting in an awakening, however,

the diary did specifically ask the reason for each awakening, options being- to use the bathroom, due to noises, due to discomfort or physical complaint, due to another or no special reason. Diaries were used to stratify subjects with and without nocturia; those reporting at least 14 nighttime awakenings to void in their 14-day sleep diary were included in this analysis (Figure 1). The primary outcome measure in our analysis was the change in self-reported nocturnal awakenings to void based on the 14-day sleep diary completed by participants pre-intervention and in the final 2 weeks of the intervention period.

Sleep was assessed using the Pittsburgh Sleep Quality Index (PSQI)²⁰ as a measure of subjective sleep quality. As an objective measure of sleep-wake patterns, 14-day wrist actigraphy data (Actiwatch-64; Minimitter, Bend, Oregon) was collected concurrently with the sleep diaries. One-minute epochs were analyzed with Actiware software, version 5.04 using sleep diary data to identify bed time and wake time. Actigraphy assessed variables analyzed in the present report include total sleep time (TST), wakefulness after sleep onset (WASO), sleep efficiency (SE) and fragmentation index (Frag). WASO was used to determine the relationship between self-reported nocturnal awakening to void and an objective measure of sleep disturbance.

Quality of life was assessed using the general health, and physical health component scores of the Medical Outcome Study 36-Item Short Form Health Survey (SF-36).²¹

Demographic information included age and sex. Medical status was evaluated based on response to a comorbidity questionnaire adapted from the Charlson Comorbidity Index,^{22, 23} with an expanded range of health conditions including hypertension, hyperlipidemia, cardiovascular disease, diabetes, and genitourinary conditions. Medication use was collected via clinician interview and medications were classified into 15 categories; we examined those relevant to nocturia, including cardiac drugs, anti-hypertensives, and diuretics.

Statistical Analysis

We used independent sample *t*- and chi-square tests respectively to compare continuous and categorical participant characteristics and baseline measures between the two intervention arms. The primary dependent variable used in our analysis is a within-subject change in the count variable- self-reported nocturnal awakenings to void. We used a histogram and probability plots to graphically check the shape of distribution and found it to be approximately normally distributed. As a sensitivity analysis, we also conducted non-parametric tests, which are not contingent on data being normally distributed, and the results did not change meaningfully, therefore we are reporting results of paired sample *t*-tests used to measure the statistical significance of pre- to post-intervention change in each of the two arms and independent sample *t*-tests used to make unadjusted comparisons between intervention arms of pre- to post-intervention change.

We also fitted analysis of covariance models using pre- to post-intervention change in each outcome as the dependent variable; intervention arm as the main factor of interest; and the baseline value of each outcome as a covariate to obtain adjusted comparisons between the intervention arms. Effect sizes were computed as standardized means differences and interpreted as 0.2–0.3=small, 0.5–0.6=moderate and 0.8–0.9=large using Cohen's (1977)

criteria. SAS version 9.3 (SAS Institute, Inc., Cary, North Carolina) was used for all statistical analyses.

RESULTS

Baseline

Table 1 displays participants' baseline characteristics, pertinent medical conditions and medication use patterns. At baseline, subjects in the two groups were comparable in age, BMI, medical conditions, and medication use. There were significantly more males in the BBTI group (43% vs. 19%), and the BBTI group also had an overall higher prevalence of genito-urinary disorders at baseline (86% vs. 31%) – the most common genito-urinary disorders were self-reported frequency, urge, and incontinence (9/12 in BBTI and 4/5 in IC), and prostatic enlargement (5/12 in BBTI and 2/5 in IC). Other GU disorders as reported by the participants were elevated prostatic specific antigen, erectile dysfunction, and nephrolithiasis.

At baseline, nocturia status was comparable for both groups: the average number of self-reported nighttime awakenings to void (summed over the 14 nights) among the IC group was 20.4 [s.d., 7.4], compared to 20.4 [s.d., 7.7] ($p=0.9$) in the BBTI group.

Response to BBTI

A significant reduction in self-reported nocturnal awakenings to void was observed in the BBTI group post-intervention (Table 2). Following BBTI, there was a 31% decrease in the mean number of awakenings to void per 14-day sleep diary ($\bar{x} = -6.5$, s.d. = 4.8, $t_{12} = -4.7$, $p < 0.01$). No decrease was observed in the IC group ($\bar{x} = +1.3$ [s.d., 7.3] per 14-day sleep diary, $t_{15} = 0.4$, $p = 0.71$). The unadjusted difference between BBTI and IC groups in pre- to post-intervention change was statistically significant $p = 0.04$ ($t_{27} = 2.2$), with a large effect size 0.82. After adjusting for the baseline frequency of nocturia, the between-group difference (SE) in nocturia frequency in BBTI versus IC was -7.7 (3.8), and remained statistically significant ($F_{1, 26} = 4.1$; $p = 0.05$ Table 2).

Concurrent with the improvement in self-reported nocturia seen in the BBTI group post-intervention, there was a significantly greater improvement in sleep quality as assessed by PSQI as well (Table 2). The BBTI group also experienced improvement in WASO and sleep efficiency as computed from actigraphy measures. Fragmentation index, as assessed by actigraphy, did not differ significantly between the groups. General health perception and the physical component of the medical outcome survey (MOS) also showed no significant group differences.

DISCUSSION

In the primary study, older adults with chronic insomnia treated with BBTI showed a significant improvement in sleep outcomes at 4 weeks compared with participants treated with IC.¹⁷ The results from this secondary analysis also reveal that BBTI has an impact on self-reported nocturia among older adults with concurrent insomnia. Not only did nocturia improve, but also sleep quality, as evident by improved PSQI scores, which is consistent

with the original study findings.¹⁷ These findings suggest that behavioral interventions directed solely at insomnia may also improve nocturia.

There are several possible explanations for these findings. First, BBTI consolidates sleep, decreases awakenings and hence, reduces nocturia as a side-effect of awakening from sleep. Elderly patients with insomnia may have awakenings due to insomnia, and may elect to void since they perceive a full bladder. From this perspective, reductions in nocturia may represent an added benefit of BBTI related improvements in the consolidation of sleep. Second, this could be a reflection of decrease in time spent in bed. Prolonged sleep duration has been shown to be an independent factor contributing to nocturia²⁴ and thus sleep restriction component of BBTI may be the key factor in nocturia improvement in this cohort. But the sleep duration at baseline in this study (380 ± 50.8 minutes) was lower than what has been used as “prolonged sleep duration” in other studies (≥ 80 minutes).²⁴ Third, by decreasing awakenings, BBTI may restore circadian rhythmicity of plasma renin activity (PRA) and decrease nocturnal urinary volume and thus nocturia. Renal excretion follows a well-defined circadian rhythm. This circadian pattern is regulated by the renin angiotensin aldosterone system (RAAS).^{25, 26} Renin release shows circadian rhythmicity, but the studies seeking to characterize a circadian rhythm for plasma renin activity (PRA) have reported conflicting results. There is evidence that PRA is driven by the sleep-wake cycle and may not be an independent circadian process: there is strong concordance between nocturnal oscillations in PRA and the rapid eye movement (REM) and non-REM (NREM) sleep cycles, with increasing PRA observed during NREM sleep periods and declining PRA levels with REM sleep periods.^{27, 28} Moreover, sleep deprivation suppresses RAAS²⁹ and induces natriuresis and diuresis in healthy children and adults,^{29, 30} indicating that sleep may play an additional important role in this interplay of physiologic processes that lead to nocturnal polyuria (NP) and hence nocturia. Thus another explanation for our findings could be that BBTI's impact on sleep leads to improvement in nocturnal polyuria and its downstream effects on nocturia. However, we do not have urinary frequency-volume charts (FVC) to evaluate this possibility.

Several studies have explored the efficacy of pharmacological agents and multicomponent behavioral interventions for nocturia, but this is the first study, to our knowledge, to examine the effect of behavioral management of insomnia on nocturia. Most of the published data for pharmacological interventions shows a statistically significant reduction in nocturnal awakenings to void following pharmacotherapy but the clinical significance of such changes has never been assessed. Commonly studied drugs include tamsulosin,^{31, 32} terazosin, finasteride, and combinations of these drugs³³ for patients with lower urinary tract symptoms; antimuscarinics for patients with overactive bladder (OAB);^{34–37} and desmopressin^{38–40} for patients with nocturnal polyuria. Each of these studies demonstrated a statistically significant benefit for nocturia with a mean reduction of 0.18 to 0.6 voids per night, and a percent reduction of 13–25%; desmopressin showed a reduction of 1.25 to 1.3 voids per night (38–45%). Behavioral intervention trials have focused on restricting fluid intake,¹⁵ moderate daily exercise, keeping warm in bed,¹⁶ pelvic floor exercises, urge suppression techniques, delayed voiding,¹³ and increased support and education from nurse practitioners.¹⁴ These studies have shown reduction in nocturia from 25–32%. Our participants reported a mean reduction of 0.46 voids per night i.e. 31% by behavioral

therapy of insomnia alone, which is comparable to pharmacologic and multicomponent behavioral therapy. Although this may appear to be a small improvement, changes in self-reported nocturia need to be considered in the context of our inclusion criteria. We included all participants who met the ICS definition of nocturia i.e. 1 void per night, rather than including only those with 2–3 voids per night at baseline as was done in all the aforementioned studies. This suggests that our findings may actually be conservative, given that a larger number of voids per night allows for greater magnitude of improvement.

Pharmacological agents used in the treatment of nocturia usually have deleterious side-effects in the elderly, eg. anticholinergic side-effects associated with antimuscarinics and hypotension caused by alpha blocking agents which can limit their use in a geriatric population. Desmopressin-induced hyponatremia, which increases in frequency with age, can be serious and makes desmopressin particularly problematic for patients aged 65 years.⁴¹ Behavioral therapies pose no such risk.

This study has several strengths. As previously noted, we included all participants who met the ICS definition of nocturia rather than those with 2 voids/ night who have a better chance of showing an improvement. Thus, our findings may be more generalizable to the entire population of individuals with nocturia. Participants were community-dwelling older adults with comorbidity profiles similar to that seen in a geriatric clinic population, which further increases the study's generalizability. Importantly, the effects observed were comparable to those seen in studies of commonly used pharmacologic agents.

Our study also has some limitations. First, unmeasured confounders could have affected the association detected between BBTI and improvement in nocturia. Small sample size (n=30) limited our ability to use relevant covariates in our analysis, thus we used the baseline value of each outcome as summary marker for relevant participant characteristics. Second, the primary outcome of the parent study focused on insomnia, and thus the study was neither designed nor powered to detect significant improvements in nocturia. Despite this limitation, large effect sizes were observed. Third, although the primary study was an RCT, the intervention groups were not perfectly matched for nocturia-relevant parameters, likely because nocturia and genito-urinary problems were not the focus of the primary study. However, nocturia was comparable between groups. Moreover, although behavioral measures targeted at lower urinary tract can improve nocturia,^{13–16} the higher prevalence of genito-urinary disorders in the BBTI group would have likely limited our ability to detect an improvement. Our analysis cohort also had a gender mismatch, but in large epidemiological studies, among older adults, nocturia was found to be equally prevalent in both males and females.^{42, 43} Fourth, participants were included in this analysis based on sleep-diary report of nocturia and not frequency-volume charts (FVC). Since the nighttime awakenings were reported the following morning, it is likely to be a reliable source of self-reported nocturia in the participants. However, because the participants did not present with the complaint of nocturia, and in absence of FVC, their daytime voiding habits were not known nor was their nighttime urinary excretion, so we cannot explore whether the response to BBTI differed among those with nocturnal polyuria. Finally, all participants had chronic insomnia with comorbid nocturia. This raises the question of whether BBTI would prove equally efficacious in patients with nocturia but without insomnia. Further studies are needed in

order to answer this question which will help elucidate the complex pathophysiology and management of nocturia in older adults.

CONCLUSION

Nocturia and sleep are inextricably linked. Therefore, the approach to a patient complaining of either condition should address both. Further controlled trials are warranted to determine whether BBTI, which is focused on consolidating sleep, may also be efficacious for nocturia in older adults without insomnia but who, nevertheless, exhibit decreases in sleep consolidation.

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REFERENCES

1. Van Kerrebroeck P, Abrams P, Chaikin D, et al. The standardization of terminology in nocturia: report from the standardization subcommittee of the International Continence Society. *BJU international*. 2002; 90(Suppl 3):11–15. [PubMed: 12445092]
2. Irwin DE, Milsom I, Hunskaar S, et al. Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: results of the EPIC study. *European urology*. 2006; 50:1306–1314. discussion 1314–1305. [PubMed: 17049716]
3. Bliwise DL, Foley DJ, Vitiello MV, Ansari FP, Ancoli-Israel S, Walsh JK. Nocturia and disturbed sleep in the elderly. *Sleep medicine*. 2009; 10:540–548. [PubMed: 18703381]
4. Asplund R, Aberg H. Health of the elderly with regard to sleep and nocturnal micturition. *Scandinavian journal of primary health care*. 1992; 10:98–104. [PubMed: 1641529]
5. Foley DJ, Monjan AA, Brown SL, Simonsick EM, Wallace RB, Blazer DG. Sleep complaints among elderly persons: an epidemiologic study of three communities. *Sleep*. 1995; 18:425–432. [PubMed: 7481413]
6. Dijk DJ, Duffy JF, Czeisler CA. Age-related increase in awakenings: impaired consolidation of nonREM sleep at all circadian phases. *Sleep*. 2001; 24:565–577. [PubMed: 11480654]
7. Dijk DJ, Duffy JF, Riel E, Shanahan TL, Czeisler CA. Ageing and the circadian and homeostatic regulation of human sleep during forced desynchrony of rest, melatonin and temperature rhythms. *The Journal of physiology*. 1999; 516(Pt 2):611–627. [PubMed: 10087357]
8. Schnelle JF, Cruise PA, Alessi CA, Al-Samarrai N, Ouslander JG. Individualizing nighttime incontinence care in nursing home residents. *Nursing research*. 1998; 47:197–204. [PubMed: 9683114]
9. Zepelin H, McDonald CS, Zammit GK. Effects of age on auditory awakening thresholds. *Journal of gerontology*. 1984; 39:294–300. [PubMed: 6715806]
10. Endeshaw YW, Johnson TM, Kutner MH, Ouslander JG, Bliwise DL. Sleep-disordered breathing and nocturia in older adults. *Journal of the American Geriatrics Society*. 2004; 52:957–960. [PubMed: 15161461]
11. Riemann D, Spiegelhalder K, Feige B, et al. The hyperarousal model of insomnia: a review of the concept and its evidence. *Sleep medicine reviews*. 2010; 14:19–31. [PubMed: 19481481]
12. Van Kerrebroeck PE, Dmochowski R, FitzGerald MP, et al. Nocturia research: current status and future perspectives. *Neurourology and urodynamics*. 2010; 29:623–628. [PubMed: 20432325]

13. Burgio KL, Goode PS, Johnson TM, et al. Behavioral versus drug treatment for overactive bladder in men: the Male Overactive Bladder Treatment in Veterans (MOTIVE) Trial. *Journal of the American Geriatrics Society*. 2011; 59:2209–2216. [PubMed: 22092152]
14. Cho SY, Lee SL, Kim IS, Koo DH, Kim HJ, Oh SJ. Short-term effects of systematized behavioral modification program for nocturia: a prospective study. *Neurourology and urodynamics*. 2012; 31:64–68. [PubMed: 21826726]
15. Hashim H, Abrams P. How should patients with an overactive bladder manipulate their fluid intake? *BJU international*. 2008; 102:62–66. [PubMed: 18284414]
16. Soda T, Masui K, Okuno H, Terai A, Ogawa O, Yoshimura K. Efficacy of nondrug lifestyle measures for the treatment of nocturia. *The Journal of urology*. 2010; 184:1000–1004. [PubMed: 20643422]
17. Buysse DJ, Germain A, Moul DE, et al. Efficacy of brief behavioral treatment for chronic insomnia in older adults. *Archives of internal medicine*. 2011; 171:887–895. [PubMed: 21263078]
18. Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR). 4th ed. Washington, DC: American Psychiatric Association; 2000. Text Revision ed.
19. Monk TH, Reynolds CF, Kupfer DJ, et al. The Pittsburgh Sleep Diary. *Journal of sleep research*. 1994; 3:111–120.
20. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry research*. 1989; 28:193–213. [PubMed: 2748771]
21. McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Medical care*. 1993; 31:247–263. [PubMed: 8450681]
22. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *Journal of chronic diseases*. 1987; 40:373–383. [PubMed: 3558716]
23. Katz JN, Chang LC, Sangha O, Fossel AH, Bates DW. Can comorbidity be measured by questionnaire rather than medical record review? *Medical care*. 1996; 34:73–84. [PubMed: 8551813]
24. Udo Y, Nakao M, Honjo H, Ukimura O, Kitakoji H, Miki T. Sleep duration is an independent factor in nocturia: analysis of bladder diaries. *BJU international*. 2009; 104:75–79. [PubMed: 19220250]
25. Kala R, Fyhrquist F, Eisalo A. Diurnal variation of plasma angiotensin II in man. *Scandinavian journal of clinical and laboratory investigation*. 1973; 31:363–365. [PubMed: 4357530]
26. Portaluppi F, Vergnani L, Tarroni G, Gilli P, degli Uberti EC. Circadian rhythms of atrial natriuretic peptide and blood pressure are consistently blunted in chronic renal failure. *Contributions to nephrology*. 1993; 101:37–43. [PubMed: 8467686]
27. Brandenberger G, Follenius M, Goichot B, et al. Twenty-four-hour profiles of plasma renin activity in relation to the sleep-wake cycle. *Journal of hypertension*. 1994; 12:277–283. [PubMed: 8021481]
28. Brandenberger G, Follenius M, Muzet A, Ehrhart J, Schieber JP. Ultradian oscillations in plasma renin activity: their relationships to meals and sleep stages. *The Journal of clinical endocrinology and metabolism*. 1985; 61:280–284. [PubMed: 3891771]
29. Kamperis K, Hagstroem S, Radvanska E, Rittig S, Djurhuus JC. Excess diuresis and natriuresis during acute sleep deprivation in healthy adults. *American journal of physiology Renal physiology*. 2010; 299:F404–F411. [PubMed: 20519376]
30. Mahler B, Kamperis K, Schroeder M, Frokiaer J, Djurhuus JC, Rittig S. Sleep deprivation induces excess diuresis and natriuresis in healthy children. *American journal of physiology Renal physiology*. 2012; 302:F236–F243. [PubMed: 22012805]
31. Robinson D, Cardozo L, Terpstra G, Bolodeoku J, Tamsulosin Study G. A randomized double-blind placebo-controlled multicentre study to explore the efficacy and safety of tamsulosin and tolterodine in women with overactive bladder syndrome. *BJU international*. 2007; 100:840–845. [PubMed: 17822465]
32. Speakman M. Efficacy and safety of tamsulosin OCAS. *BJU international*. 2006; 98:13–17.

33. Johnson TM 2nd, Jones K, Williford WO, Kutner MH, Issa MM, Lepor H. Changes in nocturia from medical treatment of benign prostatic hyperplasia: secondary analysis of the Department of Veterans Affairs Cooperative Study Trial. *The Journal of urology*. 2003; 170:145–148. [PubMed: 12796667]
34. Chapple CR, Martinez-Garcia R, Selvaggi L, et al. A comparison of the efficacy and tolerability of solifenacin succinate and extended release tolterodine at treating overactive bladder syndrome: results of the STAR trial. *European urology*. 2005; 48:464–470. [PubMed: 15990220]
35. Dmochowski RR, Peters KM, Morrow JD, et al. Randomized, double-blind, placebo-controlled trial of flexible-dose fesoterodine in subjects with overactive bladder. *Urology*. 2010; 75:62–68. [PubMed: 19931895]
36. Herschorn S, Swift S, Guan Z, et al. Comparison of fesoterodine and tolterodine extended release for the treatment of overactive bladder: a head-to-head placebo-controlled trial. *BJU international*. 2010; 105:58–66. [PubMed: 20132103]
37. Nitti VW, Dmochowski R, Sand PK, et al. Efficacy, safety and tolerability of fesoterodine for overactive bladder syndrome. *The Journal of urology*. 2007; 178:2488–2494. [PubMed: 17937959]
38. Lose G, Lalos O, Freeman RM, van Kerrebroeck P, Nocturia Study G. Efficacy of desmopressin (Minirin) in the treatment of nocturia: a double-blind placebo-controlled study in women. *American journal of obstetrics and gynecology*. 2003; 189:1106–1113. [PubMed: 14586363]
39. Mattiasson A, Abrams P, Van Kerrebroeck P, Walter S, Weiss J. Efficacy of desmopressin in the treatment of nocturia: a double-blind placebo-controlled study in men. *BJU international*. 2002; 89:855–862. [PubMed: 12010228]
40. van Kerrebroeck P, Rezapour M, Cortesse A, Thuroff J, Riis A, Norgaard JP. Desmopressin in the treatment of nocturia: a double-blind, placebo-controlled study. *European urology*. 2007; 52:221–229. [PubMed: 17280773]
41. Resnick, NM.; Tadic, SD.; Yalla, SV. Geriatric incontinence and voiding dysfunction. In: Wein, AJ.; Kavoussi, LR.; Novick, AC.; Partin, AW.; Peters, CA., editors. *Campbell-Walsh urology*. 10th edn.. Philadelphia, PA: Elsevier Saunders; 2012. p. 2204-2222.
42. Bosch JL, Weiss JP. The prevalence and causes of nocturia. *The Journal of urology*. 2010; 184:440–446. [PubMed: 20620395]
43. Weiss JP, Blaivas JG, Bliwise DL, et al. The evaluation and treatment of nocturia: a consensus statement. *BJU international*. 2011; 108:6–21. [PubMed: 21676145]

Figure 1. Analytic Design

Notes: Shaded boxes indicate participants included in the current analysis

Table 1

Baseline Demographics and Clinical Characteristics of Patients with Nocturia

Characteristics	BBTI (n=14)	IC (n=16)	p-value
Age, y (sd)	74.1 (6.4)	73.1 (7.9)	.69
Female, n(%)	8 (57)	13 (81)	.03
BMI (sd)	25.7 (2.4)	25.5 (2.7)	.75
Nocturia, episodes/14-day sleep diary (sd)	20.4 (7.7)	20.4 (7.4)	.94
Medical conditions, n (%)			
Diabetes	2 (14)	1 (6)	.58
Cardiovascular disease	3 (21)	7 (44)	.08
Hypertension	6 (43)	7 (44)	.56
Arthritis	12 (86)	12 (75)	.42
Genito-urinary disorder	12 (86)	5 (31)	<.01
Medication use, n (%)			
Anti-hypertensives	5 (36)	7 (44)	.51
Diuretics	1 (7)	1 (6)	.9
Other cardiac medications	5 (36)	7 (44)	.51
Analgesics	14 (100)	14 (88)	.18

Table 2

Baseline Status and Post intervention Outcomes by Treatment Group

	BBTI (n=14)		IC (n=16)		Adjusted group difference (SE)	f statistic and DF	p value
	Pre mean(SD)	Post mean(SD)	Pre mean(SD)	Post mean(SD)			
Nocturia	20.4 (7.7)	13.9 (6.9) *	20.4 (7.4)	21.7 (7.9)	-7.7(3.8)	4.1 1, 26	.05
Total sleep time(minutes)	378.4 (40.8)	332.4 (26.0) *	384.2 (32.4)	365.1(55.6)	-25.7 (13.1)	3.9 1, 17	.06
WASO (minutes)	60.4 (23.4)	47.2(22.4) *	60.1 (26.5)	57.1(15.7)	-10.7 (5.2)	4.2 1, 17	.05
Sleep efficiency (%)	78.9 (8.7)	82.3 (6.5) *	81.2 (5.5)	79.6 (6.3)	3.5 (1.9)	3.3 1, 17	.08
Fragmentation index	34.8 (10.7)	29.5 (11.0)	32.1 (9.9)	31.8 (8.4)	-1.7 (3.3)	0.3 1, 17	.60
PSQI	10.8 (3.2)	7.5 (3.4) *	10.3 (3.3)	9.5 (2.8)	-2.3 (0.9)	6.1 1, 26	.02
MOS general health	69.4 (14.38)	72.9 (13.5) *	66.8 (21.4)	66.7 (19.7)	3.0 (3.2)	0.9 1, 25	.29
MOS physical component score	43.8 (7.8)	45.4 (7.9)	44.5 (12.9)	41.1 (12.6)	3.0 (2.1)	2.2 1, 24	.15

Notes:

* Within group pre- to post-intervention change, p 0.05

Adjusted group difference: adjusted for the baseline value of outcome

WASO= Wakefulness after sleep onset, PSQI= Pittsburgh Sleep Quality Index, MOS = Medical Outcome Survey